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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,923	03/10/2004	Kenneth W. Dobie	RTS-0739US	9182

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EXAMINER	
ASHEN, JON BENJAMIN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/798,923	DOBIE ET AL.	
	Examiner	Art Unit	
	Jon B. Ashen	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-30 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-30 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth below. Page 54 of the specification discloses nucleotide sequences that lack associated SEQ ID NO's. Appropriate correction is required in response to this action and must be included as part of any response to a restriction requirement.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 2-16, 21, 26-30 are drawn to a compound 8-80 nucleobases in length that inhibits the expression of ACE2 mRNA, classified in class 536, subclass 24.5.

II. Claims 17 and 22-23 are drawn to a method of treating an animal by inhibiting the expression of ACE2 in cells or tissues, classified in class 514, subclass 44.

III. Claims 18-19 are drawn to a method of screening for a modulator of ACE2, classified in class 435, subclass 6.

IV. Claim 20 is drawn to a method for identifying the presence of ACE2 in a sample, classified in class 435, subclass 91.2.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions of group I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). The invention of group I is drawn to a compound 8-80 nucleobases in length that inhibits the expression of ACE2. The invention of group II is drawn to a method of treating an animal by inhibiting the expression of ACE2 in cells or tissues. In the instant case, the product that is the invention of group I can be used in a materially different process of using that product; e.g., a hybridization assay for determining tissue-specific gene expression, for example. Therefore, the inventions of group I and II are related as product and process of use.

3. Inventions of groups I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The invention of group I is drawn to a compound 8-

80 nucleobases in length that inhibits the expression of ACE2. The invention of group III is drawn to a method of screening for a modulator of ACE2. In the instant case the different inventions are not disclosed as capable of use together and have different functions. The invention of group I functions to inhibit the expression of ACE2. The invention of group III functions to identify compounds capable of modulating the expression of ACE2. Therefore, the inventions of group I and group III are unrelated.

4. Inventions of groups I and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The invention of group I is drawn to a compound 8-80 nucleobases in length that inhibits the expression of ACE2. The invention of group IV is drawn to a method for identifying the presence of ACE2 in a sample. In the instant case the different inventions are not disclosed as capable of use together and have different functions. The invention of group I functions to inhibit the expression of ACE2. The invention of group IV functions to identify the presence of ACE2 in a sample. Therefore, the inventions of groups I and IV are unrelated.

5. Inventions of groups II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP

§ 806.04, MPEP § 808.01). The invention of group II is drawn to a process of inhibiting the expression of ACE2 using a compound that inhibits the expression of ACE2. The invention of group III is drawn to a method of screening for a modulator of ACE2. In the instant case the different inventions are not disclosed as capable of use together and have different functions. The invention of group II functions to inhibit the expression of ACE2. The invention of group III functions to identify compounds capable of modulating the expression of ACE2. Therefore, the inventions of groups II and III are unrelated.

6. Inventions of groups II and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The invention of group II is drawn to a method of treating an animal by inhibiting the expression of ACE2 in cells or tissues. The invention of group IV is drawn to a method for identifying the presence of ACE2 in a sample. In the instant case the different inventions are not disclosed as capable of use together and have different functions. The invention of group II functions to inhibit the expression of ACE2. The invention of group IV functions to identify the presence of ACE2 in a sample. Therefore, the inventions of groups I and IV are unrelated.

7. Inventions of groups III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they

have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The invention of group III is drawn to a method of screening for a modulator of ACE2. The invention of group IV is drawn to a method for identifying the presence of ACE2 in a sample. In the instant case the different inventions are not disclosed as capable of use together and have different functions. The invention of group III functions to identify compounds capable of modulating the expression of ACE2. The invention of group IV functions to identify the presence of ACE2 in a sample. Therefore, the inventions of groups III and IV are unrelated.

8. Groups I and IV are further restricted as follows:

Pursuant to 35 U.S.C. 121 and 37 C.F.R. 1.141, the oligonucleotide and antisense sequences listed in claims 21, 25 and 26 are subject to restriction. The Commissioner has partially waived the requirements of 37 C.F.R. 1.141 and will permit a reasonable number of such nucleotide sequences to be claimed in a single application. Under this policy, up to 10 of independent and distinct nucleotide sequences will be examined in a single application. (see MPEP 803.04 and 2434)

Claim 20 specifically claims a method of identifying the presence of ACE2 in a sample using at least one of SEQ ID NO's 5-7. Although the instant oligonucleotide sequences claimed in claim 20 each target the same gene, the instant oligonucleotide sequences are considered to be unrelated, since each oligonucleotide sequence claimed is structurally and functionally independent

and distinct for the following reasons: each oligonucleotide sequence has a unique oligonucleotide sequence, each oligonucleotide sequence targets a different and specific region of ACE2, and each oligonucleotide upon binding to ACE2, will act as either a forward or reverse PCR primer (SEQ ID NO: 5-6) or as a hybridization probe (SEQ ID NO: 7).

Further, MPEP 808.02 states in part:

Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05(C) - 806.05(i), the examiner, in order to establish reasons for insisting upon restriction, must shown by appropriate explanation one of the following:

(C) A different field of search: Where it is necessary to search for one of the distinct subjects in places where no pertinent art to the other subject exists, a different field of search is shown, even though the two are classified together.

It is noted that a search of the available sequence databases produces a listing of references disclosing the sequence most similar to the query sequence. This is the "place" where the examiner searches for prior art. The prior art relating to another query sequence will not be found in this "place"- a different listing of references must be generated and searched by the examiner. Thus a different search is shown, and restriction is proper.

Claims 24 and 25 specifically claim a compound 8-80 nucleobases in length targeted to a nucleic acid molecule encoding ACE2, comprising SEQ ID NO's 14-16, 18-24, 26, 28-30, 32-38, 40, 42-43, 45-46, 49-53, 55-71, 73-74,76-78, 80, 82, 86 or 88-90. Although the instant antisense sequences claimed in 24

and 25 each target the same gene, the instant antisense sequences are considered to be unrelated, since each antisense sequence claimed is structurally and functionally independent and distinct for the following reasons: each antisense sequence has a unique nucleotide sequence, each antisense sequence targets a different and specific region of ACE2, and each antisense sequence, upon binding to ACE2, functionally decreases the expression of the gene to varying degree (per applicants' Table 1 in the specification). Applicant is required to identify which of claims 26-30, linked by claim 1, corresponds to the elected SEQ ID NO.

Furthermore, a search of more than one (1) of the instant sequences presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the instant sequences and for the reasons cited above. In view of the foregoing, one (1) nucleotide sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicant is required to elect one oligonucleotide (1) sequence from claims 20, 24 or 25 that corresponds to the target region claimed. This sequence will be examined based on the group elected.

9. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and would require divergent searches of sequence and literature databases placing

an undue administrative burden on the examiner, restriction for examination purposes as indicated is proper.

10. Claim 1 link(s) the various inventions of group I that are the individual antisense oligonucleotide sequences listed in claims 24 and 25 (that are SEQ ID NO's: 14-16, 18-24, 26, 28-30, 32-38, 40, 42-43, 45-46, 49-53, 55-71, 73-74,76-78, 80, 82, 86 or 88-90) and also the inventions of claims 26-30. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 1. Claims 1 and 26-30 link the various inventions of claims 24 and 25 that are the individual antisense oligonucleotide sequences listed. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

11. Claims 2-16, 21, 26-30 are generic to group 1 which links the inventions of claims 25 and 26 that are SEQ ID NO's: 14-16, 18-24, 26, 28-30, 32-38, 40, 42-43, 45-46, 49-53, 55-71, 73-74,76-78, 80, 82, 86 or 88-90.

12. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and

Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

13. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0670. The

fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jba